DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

Office of Technology Transfer
National Institutes of Health
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Commissioner of Patents and Trademarks
Patent and Trademark Office
Washington D.C. 20231

Attention: Scott A. Chambers, Associate Solicitor

Supplemental Comments on Interim Guidelines on the Written Description Requirement

The written comments presented herein supplement the written comments provided September 14, 1998 and the oral testimony presented November 4, 1998. A transcript of the oral testimony is submitted with this document. These comments represent the views of the National Institutes of Health (NIH). The NIH is the lead agency within the Public Health Service (PHS) in matters of technology transfer. In addition to providing patent and licensing services to all Institutes and Centers comprising the NIH, PHS lead agency status encompasses coordinating and facilitating technology transfer policy functions with the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA). Central responsibility for these technology transfer functions has been delegated to the Office of Technology Transfer (OTT), NIH.

November 9, 1998 Meeting

The NIH expresses its appreciation for the meeting of November 9, 1998 between the NIH and Commissioner Bruce Lehman, Deputy Commissioner Q. Todd Dickinson, Acting Solicitor Albin Drost, and Dr. Scott Chambers, Associate Solicitor. The NIH was represented by Dr. Harold Varmus, Director, NIH; Dr. Francis Collins, Director, National Human Genome Research Institute; Dr. Maria Freire, Director, OTT; and Dr. Jack Spiegel, Director, Division of Technology Development and Transfer within the OTT. The discussion at this meeting included the vision of the NIH regarding the development of genomic research, and the potential impact of patents of different variety and scope on that developmental process. Subsequent to that meeting, the NIH was made aware of patent 5,817,479 (‘479 patent) issued October 6, 1998 to Incyte Pharmaceuticals, Inc., for Human Kinase Homologs. Issues raised about this patent serve to focus some of the concerns addressed in our September 14th written comments, our November 4th oral testimony, and the November 9th meeting.

Background for the ‘479 Patent

The ‘479 patent discloses a series of partial cDNA sequences derived from genes coding for one or more proteins belonging to the family of protein kinases. The specification defines these kinases as “…the largest known protein family, a superfamily of enzymes with widely varied functions and specificities.” These kinases are described as regulating many different cell proliferation, differentiation, and signalling processes by adding phosphate groups to proteins. Indeed, the specification states that “[r]eversible protein phosphorylation is the main strategy for controlling activities of eukaryotic cells.”

The specification discloses a number of general utilities such as hybridization probes for chromosomes and gene mapping. Also disclosed are other research utilities associated with altered expression of the complete kinase protein such as production of antisense molecules, screening for new therapeutic molecules, and assays for associated diseases. Prophetic examples are provided describing standard genetic engineering and molecular biology techniques in support of such utilities. One full length sequence for a MAP kinase is disclosed (SEQ ID NO: 45), but not claimed. A generalized procedure is exemplified to extend one partial cDNA sequence (SEQ ID NO: 38) to obtain that full length sequence.

There are four claims. The first claim is of the form “[A] purified polynucleotide having a nucleic acid sequence selected from the group consisting of …”. A Markush group of all 44 disclosed sequence fragments is then enumerated by their SEQ ID NO:. Claim 2 is to an expression vector comprising the polynucleotide of claim 1. Claim 3 is to a host cell transformed with the expression vector of claim 2. The final claim is to a method for producing and purifying a polypeptide that recites two steps. The first step is to culture host cells according to claim 3 under conditions suitable for expression of the peptide. The second step involves recovering the polypeptide from the host cell culture.

Scope of ’479 Claims

The scope of claims 2-4 derive from the scope afforded to each of the Markush group polynucleotide sequences of claim 1 by the “having” transition term. The MPEP at Section 2111.03 instructs that the transition term “having” must be interpreted in light of the specification to determine whether “open” or “closed” claim language is intended. While the specification does not specifically address the term “having”, column 8, lines 45-56 sets forth an indication of the intended scope of the invention.

> As a result of the degeneracy of the genetic code, a multitude of kinase-encoding nucleotide sequences may be produced and some of these will bear only minimal homology to the endogenous sequence of any known and naturally occurring kinase. This invention has specifically contemplated each and every possible variation of nucleotide sequence that could be made by selecting combinations based on possible codon

> choices. These combinations are made in accordance with the standard triplet genetic code as applied to the nucleotide sequence of naturally occurring kinases, and all such variations are to be considered as being specifically disclosed.

In view of the above and the doctrine of affording claims their broadest possible interpretation in light of the specification, the transition term "having" must be interpreted as an "open" claim format Therefore, "having" in this case is analogous to "comprising" transition language. Consequently, every full-length kinase polynucleotide that contains within its structure any of the 44 SEQ ID NO: partial sequences falls within the scope of Claim 1.

Realization of aspects of this claim scope may be appreciated by comparing the 189 base sequence of SEQ ID NO: 38 to the 1851 full-length sequence of the MAP kinase represented in Fig. 1A or SEQ ID NO: 45. Had the full-length sequence of this MAP protein kinase been disclosed after filing of the application, it still would be encompassed within the scope of Claim 1 based upon possession of SEQ ID NO: 38. In other words, possession of SEQ ID NO: 38 in Claim 1 of the '479 patent would place the inventor also in possession of the 10-fold larger full-length sequence. This leads to logical inconsistencies because of case law teachings regarding what is required to effect possession of DNA structures. *Fiers v. Sugano*[1] and *University of California v Eli Lilly*[2] teach possession of a DNA structure must be defined by its sequence or other physical properties. This case law affirmatively teaches that possession is neither defined by functionality alone nor by the availability of art-recognized means to prepare or obtain the DNA structure. By analogy to chemical practice where one skilled in the art can distinguish or envisage numerous species encompassed within a generic formula, the 1,662 additional nucleotides characteristic of SEQ ID NO: 45 must be envisaged from the structure SEQ ID NO: 38 within generic claim 1. No rational basis exists to support such an event and, therefore, no rational basis exists to support possession of the full-length structure within the scope of the claim.

The illogical conclusion that possession of a full-length nucleic acid structure follows from possession of a sequence fragment and the magical intervention of "open" claim construction is debunked further by the realization that a prior disclosure of SEQ ID NO: 38 would not render obvious a later claim to full-length sequence SEQ ID NO: 45. Again, the case law (*In re Bell*[3] and *In re Deuel*[4]) instructs that a DNA invention is not rendered obvious by knowledge of partial sequence combined with methods capable of generating or obtaining that sequence. Specifically referring to this relationship in *In re Bell* and *In re Deuel*, *California v. Lilly* states, "…a description that does not render a

[1] *Fiers v. Sugano*, 25USPQ2d 1601 (Fed. Cir. 1993)
[2] *University of California v. Eli Lilly and Co.*, 43USPQ2d 1398 (Fed. Cir. 1997)
[3] *In re Bell*, 26USPQ2d 1529 (Fed. Cir. 1993)
[4] *In re Deuel*, 34USPQ2d 1210 (Fed. Cir. 1995)

claimed invention obvious does not sufficiently describe that invention for purposes of ' 112, & 1."

The impropriety of this scope relationship is magnified when extended to all the unknown protein kinase genes and proteins that potentially can be encompassed and dominated by the other 43 members of the Markush group of Claim 1. The pervasive biological significance of the protein kinase family is outlined in columns 1 to 4 of the '479 patent. Patentee's contributions have modestly advanced the art by identifying probes homologous to known protein kinase sequence motifs. With the possible exception of the MAP kinase corresponding to SEQ ID NO: 45, patentee neither identified nor further characterized any new protein kinases. Similarly, patentee has not advanced knowledge in the art regarding any significant biological properties and functions of this family of proteins. Through application of "open" claim drafting, however, the patentee may exclude others from making, using, and selling any gene sequence for protein kinase enzymes containing one of the 44 SEQ ID members anywhere within the gene structure. Similarly, patentee may exclude from use any expression vector containing such future discoveries or cells containing such expression vectors. Finally, patentee may exclude from use any protein kinase enzymes made through recombinant technology using a cell or expression vector containing any of the Markush sequences.

Arguments Related to EST Claims

Such disconnect between the scope of claim protection and the scope of disclosure does not serve the *quid pro quo* upon which our patent system is based. The possibility of a chilling effect within a developing field such as genomics is a serious concern when such discordance between levels of disclosure and patent scope becomes an expectation. This situation is exacerbated when millions of ESTs are permitted to exist at the PTO in a secret submarine state, and there is an expectation that EST claims will issue with a breadth sufficient to encompass later discovered full-length gene sequences.

The capacity for an exceptionally large number of ESTs to reside in a "submarine" state can arise from a motivation to maintain ESTs in a "withdrawn from consideration" status following restriction practice. Such motivation derives from an expectation that EST claims would issue with broad "open" transition language; yet no commercial market exists until a valuable new gene is identified by others in the art.

This scenario can be circumvented through issuing patents with claims commensurate in scope with their level of disclosure (i.e., contribution to the art). Since the individual value of most anonymous EST sequences is low, NIH believes this goal is accomplished by issuing patents of commensurately narrow scope. In this regard, guidance has been provided by the Federal Circuit regarding treating DNA inventions in a manner analogous to chemical practice, such that DNA claims are defined by their specific structural or

physical characteristics. The line of decisions in *Amgen v. Chugai*[5], *Fiers v. Sugano*, *In re Bell*, *In re Deuel*, and *University of California v. Lilly* consistently focus on a narrow interpretation of DNA structure in order to satisfy considerations of enablement, written description, and obviousness.

Unlike the rest of chemical practice, the scope of DNA and protein sequence claims appears to be disproportionately influenced by the choice of "open" versus "closed" claim transition language. The use of "closed" transition language, such as "consisting of" is consistent with our belief that EST claims should be narrowly defined. The NIH believes that such claim construction is most consistent with the direction provided by the Federal Circuit. The NIH hopes the PTO appreciates the potential deleterious consequences to the development of genomics that may arise from large scale issuance of broad patents on research tool discoveries such as ESTs and SNPs. The NIH urges the PTO to consider the arguments raised regarding the relationship of "open" claim language to overly broad claim scope in the area of DNA and protein sequence claims. If the PTO feels that judicial precedent is not sufficiently established in this area, it is urged to establish a test case and expeditiously advance it to the Federal Circuit for resolution.

The controversy and importance of EST patents is sufficient in the biotechnology community to warrant treatment in the Final Guidelines on Written Description. Toward that end, the NIH requests that the PTO address the issue of EST claim scope and its relation to claim transition language.

The NIH again thanks the PTO for the cordial fora it provided for the presentation of our views. We are eager to extend whatever assistance we can provide in our common mission to advance science and technology.

/s/

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Enclosure: Transcript of Oral Testimony of November 4, 1998

[5] *Amgen Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18USPQ2d 1016 (Fed. Cir. 1991)